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New Drug Launches Worldwide Dipped In 2019

But A Higher Proportion Were First In Class

by Alex Shimmings

The number of new active substances launched in their first market in 2019 dropped as 2018's superlative performance gave way to something more usual.

There were 49 novel products introduced onto their first markets worldwide in 2019, a sharp fall from the record-breaking 68 that debuted in 2018, but a nonetheless respectable figure when viewed across the years, new research from Citeline's drug database Pharmaprojects reveals.

The launch tally last year suffered from a lack of new vaccines with novel antigenic components which in other years have boosted the tally, but if vaccines are discounted, 2019 was actually the third best year since the turn of the century (see Figure 1).

Moreover, in terms of novelty, 2019 could be deemed a better year than 2018, with a higher proportion of the new drugs being first in class, ie, those with mechanisms of action that have not previously been seen in a marketed drug (28.6% vs 25.0%).

The Citeline research focuses exclusively on new active substances (NASs): new chemical or biological entities where the active ingredient had received no prior approval for human use, and excludes the 91 new drug launches last year with reformulated or non-NAS moieties, or biosimilars.

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As Figure 1 shows, without counting vaccines, the five-year (2015–19) mean is 46.8 NAS launches per year, making 2019 a good year by comparison. Its performance was also better than

the 2010-2014 average of 40.4 NAS launches and well ahead of the 2005–09 mean of 27.4. The mean NASs per year since 2000 is 36.4.

Table 1 below gives the full alphabetical list of 2019's new drugs, including trade names, companies involved in their launch, indication and whether or not they are first-in-class, are for rare diseases, and/or had orphan drug status.

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A look at the NAS launch performance of the Top 10 companies by pipeline size (Table 2 lists these plus other companies that were involved in the introduction of more than one new drug), shows that *Novartis AG* – which boasts the largest drug pipeline – pulled away from its rivals with five new products launched. These encompassed small molecules, monoclonals and gene therapies and were approved for a range of indications.

It was also a good year for Japanese firms, with four NASs apiece from *Astellas Pharma Inc.* (each with a partner) and *Daiichi Sankyo Co. Ltd.* (one under license and three for itself). Four Top 20 companies produced two NASs each – *AbbVie Inc.*, *Roche*, *Johnson & Johnson* and *Bristol-Myers Squibb Co.*

However, three of the Top 10 pharmas by pipeline size – *Merck & Co. Inc.*, *AstraZeneca PLC* and *Pfizer Inc.* – failed to bring a single drug to the table between them (although AZ was a licensee for one new NAS's second launch). Overall, it was a worse year for the Top 10 firms as they only contributed 13 of 2019's NASs, far fewer than the 18 they produced in 2018.

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Looking at the indications served by 2019's novel products (see Figure 2), Cancer, unsurprisingly, dominates, with almost a third of all NASs being in Oncology. The tally of 16 new cancer drugs this year is one less than the 17 launched in 2018, but they make up a larger proportion of the whole and one that is closer to its overall share of the pipeline. By contrast, Anti-infectives, which matched Cancer's 17 NASs in 2018, had a much poorer year, only producing five NASs.

The neurologicals segment complemented its position in second place in terms of pipeline numbers with the second-highest number of NAS launches, at six, and tying with Blood & Clotting drugs. Almost all therapeutic areas were represented by at least one NAS launch.

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Country By Country

The choice of market for first launch may vary little from year to year in terms of the top countries, but what was new in 2019 was a sharp decline in the popularity of European markets.

The pie chart in Figure 3 shows that 29 of the 49 NASs, or 59%, debuted in the US, a similar proportion to 2018. No other country came close: Japan was again a distant second place, with 11 first launches, up from eight. China once more came in third, with five first NAS launches, one more than in the previous year.

But it is the narrowing of the field that is most arresting. 2018's NAS launches were spread across a total of 20 different markets, but last year, they occurred in just eight, and this is largely the result of a drop in European debuts. 2019 posted just one (in both Germany and the UK), compared with 14 in 2018 across a range of countries. It seems that market access complexities and strict pricing negotiations are contributing to the delay in launching drugs in Europe.

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An orphan drug designation (ODS) has an impact on the launch data in that it is accompanied, most clearly in the favored US market, by markedly shortened approval times. Analysis by our sister publication *Pink Sheet* (Also see "*CDER Reviewers Showcase Speed In 2019 With 11 Novel Drugs Approved Within Six Months*" - Pink Sheet, 6 Jan, 2020.) of US Food and Drug Administration data indicates that in 2019, drugs with ODS took on average 8.1 months to approve, compared with 30.5 months for drugs without ODS or any other form of expedited approval pathway.

Last year, 23 (47%) of the first launches targeted a rare disease, and 40.8% (20 out of 49) had received orphan drug status for the disease they were launched for in the country in which they were first marketed – a significant portion, but, as Figure 4 shows, in keeping with the proportions seen across all the past four years.

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First in class

Last year saw the launch of 14 first-in-class NASs, slightly less than in 2018 numerically, but a higher proportion of the total (28.6% vs 25.0%).

The therapeutic spread of these novel NASs is broader too. Cancer, with three novel NASs, shared its title as most innovative category with Blood & Clotting products. There are two apiece for Cardiovascular and Musculoskeletal, and one each for Alimentary/Metabolic, Dermatological, Genitourinary and Infectious Diseases.

Cancer

In Cancer, *Karyopharm Therapeutics Inc.*'s Xpovio was launched for myeloma in the US in July, and was the first example of a CRM1 nuclear exportin 1, or XPO1, inhibitor. The protein is overexpressed in several cancer types.

Xpovio has now been filed for diffuse large B-cell lymphoma in the US and is in late-stage clinical trials for multiple other cancer types.

Roche's Rozyltrek was first launched in Japan for cancers with the NTRK fusion genetic defect, and for non-small cell lung cancer. This is not the first tumor-agnostic drug – *Array BioPharma Inc.* and *Loxo Oncology Inc.*'s Vitrakvi was launched in 2018. Vitrakvi inhibits TrkA tyrosine kinase, but Rozlytrek also hits the related TrkB and TrkC (along with ROS1 and ALK), making it the first drug to inhibit TrkB or TrkC on the market.

Orion Corp. and *Bayer AG*'s Nubeqa was first launched in the US for non-metastatic castration-resistant prostate cancer back in August. This is the first selective non-steroidal androgen receptor modulator (SARM) and is taking on established androgen antagonist drugs such as enzalutamide. Bayer just reported Q1 sales for the product that it said were better than expected.

The three novel Blood & Clotting therapy area launches included two new treatments for sickle cell disease – a previously very underserved condition.

Novartis's Adakveo, first launched in the US in November, was the first P-selectin antagonist, and treats the crisis precipitated by vaso-occlusion in sickle cell anemia.

The following month it was joined on the market by *Global Blood Therapeutics Inc.*'s Oxbryta. This drug tackles sickle cell disease in a different way: it is an allosteric modifier of hemoglobin oxygen affinity, and so is classified as a hemoglobin oxygen release stimulant. Rather than treating the effects of sickle cells clogging up capillaries, it makes red blood cells deliver their oxygen more effectively.

FibroGen Inc.'s Evrenzo, the first HIF-PHI inhibitor, was launched in Japan with its licensee Astellas for anemia associated with chronic kidney disease in dialysis patients.

This drug has a number of potential competitors in the offing, including Japan Tobacco's enarodustat, *GlaxoSmithKline PLC*/*Kyowa Kirin Co. Ltd.*'s daprodustat, and *Mitsubishi Tanabe Pharma Corp.*'s vadadustat all awaiting approval, plus there are others in Phase III.

Cardiovascular

In Cardiovascular, *Ionis Pharmaceuticals Inc.* launched the antisense product Waylivra in Germany for chylomicronemia syndrome. This oligonucleotide targets apolipoprotein C3, high

levels of which induce hypertriglyceridemia, and therefore, atherosclerosis. It also inhibits lipoprotein lipase.

The therapy area also saw the launch of the gene therapy Collategene which delivers the gene for hepatocyte growth factor via a plasmid vector, and was first launched in Japan.

It was originated at *AnGes Inc.*, which teamed up with Mitsubishi Tanabe Pharma to bring the drug to market for critical limb ischemia.

It was a long journey though. The product was originally filed in Japan for arteriosclerosis obliterans and Buerger's disease back in 2008, but with no success. Persistence has paid off, and together with another product launch last year brought the number of marketed gene therapies into double figures.

Other Therapies

The other gene therapy was Novartis's Zolgensma – which it obtained through its acquisition of *AveXis Inc.* – approved and launched in June for spinal muscular atrophy (SMA).

It was not the first treatment for SMA – it competes against *Biogen Inc.*'s Spinraza – but it is the first with the promise of a one-time cure, and its sales are being closely watched. Full-year sales were $361m last year and Novartis has just reported first quarter sales of $170m – a bit lower than consensus.

The second musculoskeletal launch was for *Amgen Astellas BioPharma KK*'s Evenity (romosozumab). Launched in March in Japan for severe osteoporosis in postmenopausal women. It is the first sclerostin inhibitor; sclerostin stops bone formation and increases its breakdown.

Other first-in-class products included the second RNA interference drug to reach the market, *Alnylam Pharmaceuticals Inc.*'s Givlaari, launched in the US in December for acute hepatic porphyria. Alnylam also launched the first RNAi drug in 2018, Onpattro (patisiran).

AMAG Pharmaceuticals Inc. launched Vyleesi, for female sexual dysfunction, the first melanocortin 4 receptor agonist on the market. It was originally investigated 20 years ago by *Palatin Technologies Inc.* as a nasal spray, but a change of delivery route to an auto-injected pen led to approval for hypoactive sexual desire disorder in pre-menopausal women.

Lastly, Symbiox was launched in China for psoriasis by local firm Beijing Wenfeng Tianji Pharmaceuticals. This is an aryl hydrocarbon receptor agonist and has roles in regulating immunity and cellular differentiation. The drug is also being developed internationally being licensed to both GSK and *Japan Tobacco Inc.* are licensees.